

## TENT COOPERATION TRE.

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## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 07 April 2000 (07.04.00)	
International application No. PCT/AU99/00724	Applicant's or agent's file reference 2212294/PDB
International filing date (day/month/year) 03 September 1999 (03.09.99)	Priority date (day/month/year) 04 September 1998 (04.09.98)
Applicant BERNARD, Hans-Ulrich et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

07 March 2000 (07.03.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The international Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Juan Cruz
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**PCT**

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference 2212294/PDB/GH	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. <b>PCT/AU99/00724</b>	International Filing Date (day/month/year) 3 September 1999	Priority Date (day/month/year) 4 September 1998
International Patent Classification (IPC) or national classification and IPC  <b>Int. Cl. <sup>7</sup></b> C07D 203/24, 205/04, 207/48, 209/48, 211/96, 213/76, 239/28, 239/42, 243/08, 263/04, 265/30, 295/194, 295/26, 317/58; C07C 323/49, 333/32, 381/00; A61K 31/13, 31/145, 31/535, 31/55		
Applicant <b>INSTITUTE OF MOLECULAR AND CELL BIOLOGY et al</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.  
☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 7 sheet(s).

3. This report contains indications relating to the following items:

- |      |                                     |   |
|------|-------------------------------------|---|
| I    | <input checked="" type="checkbox"/> | Basis of the report   |
| II   | <input type="checkbox"/>            | Priority  |
| III  | <input type="checkbox"/>            | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| IV   | <input type="checkbox"/>            | Lack of unity of invention  |
| V    | <input checked="" type="checkbox"/> | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| VI   | <input type="checkbox"/>            | Certain documents cited   |
| VII  | <input type="checkbox"/>            | Certain defects in the international application  |
| VIII | <input checked="" type="checkbox"/> | Certain observations on the international application   |

CORRECTED  
VERSION

Date of submission of the demand 7 March 2000	Date of completion of the report 4 January 2001
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer  <b>CHRISTINE BREMERS</b> Telephone No. (02) 6283 2313

**I. Basis of the report**

1. With regard to the elements of the international application:\*
- ☐ the international application as originally filed.
- ☒ the description, pages **1-49** as originally filed,  
pages , filed with the demand,  
pages , received on with the letter of
- ☒ the claims, pages , as originally filed,  
pages , as amended (together with any statement) under Article 19,  
pages , filed with the demand,  
pages **50-55** received on **7 July 2000** with the letter of **7 July 2000** and  
page **56** received on **22 August 2000** with the letter of **22 August 2000**
- ☒ the drawings, pages **1/5-5/5** , as originally filed,  
pages , filed with the demand,  
pages , received on with the letter of
- ☐ the sequence listing part of the description:  
pages , as originally filed  
pages , filed with the demand  
pages , received on with the letter of
2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
These elements were available or furnished to this Authority in the following language which is:
- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, was on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished
4. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/fig.
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims 1-13, 37-38, 40	YES
	Claims 36, 39	NO
Inventive step (IS)	Claims 1-35, 37-38, 40	YES
	Claims 36, 39	NO
Industrial applicability (IA)	Claims 1-40	YES
	Claims	NO

**2. Citations and explanations (Rule 70.7)**Novelty and Inventive Step

1. Derwent Abstract 92-303542/37
2. Synlett
3. Derwent Abstract 95-340184/44
4. Brain Research
5. Derwent Abstract 86-282536/43
6. Derwent Abstract 88-245781/35
7. Derwent Abstract 91-038784/05
8. Derwent Abstract 91-122584/17
9. EP 562750
10. Virology
11. Journal of Medicinal Chemistry vol 40
12. Techniques in Protein Chemistry
13. WO 96/09406
14. Drug Metabolism and Disposition: The Biological Fate of Chemicals
15. Journal of Medicinal Chemical vol 39
16. Journal of Virology
17. Carcinogenesis
18. Chemical Abstracts 102:8009
19. Chemical Abstracts 111:146042
20. Chemical Abstracts RN 95255-69-9
21. Chemical Abstracts RN 103-34-4

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. Claim 39 is speculative. The term "an agent" as used in the claim, has been construed as meaning a compound. Thus claim 39 is a claim to any compound per se (which has the property of facilitating disruption of a chelated metal cation domain present in the protein of the claim). This goes beyond the description which only exemplifies compounds of formulas (I) and (II). Also included within the scope of the claim are compounds which are already known.

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

**Continuation of Box V**

1. D3-D16 disclose methods of treating or preventing a disease condition caused or exacerbated by HIV, by using a compound of formula(I) or (II). D10-D16 disclose the release of zinc from the zinc finger. D17 discloses a method of treating or preventing cancer by treating papillomas with disulfiram (a compound of formula(II)).

Treatment or prevention of MPV or HPV related diseases are not disclosed in D3-D17.

2. D1, D2 and D18-21 disclose compounds of formula (I) and pharmaceutical compositions thereof.

D3-D17 disclose compounds of formula (II) and pharmaceutical compositions thereof.

Also according to the description on page 29 lines 6-8, compounds C32, C35, C16 and C37 as per pages 25, 27 and 28 of the description, which are of formula (I) or (II), are known. These compounds are disclosed in D15, D4, D21 and D2 respectively.

Thus, claim 36 which is to a pharmaceutical composition comprising said compounds and claim 39 which is to the compounds per se, are not novel and lack inventive step in light of D1-D21.

- 50 -

## THE CLAIMS:

1. A method of identifying compounds useful in the treatment of a disease condition caused or exacerbated by an MPV comprising contacting a protein molecule containing a  
5 chelated metal cation domain, encoded by an MPV gene, with an effective amount of said compound for a time and under conditions sufficient to facilitate disruption of the chelated metal cation domain and directly or indirectly determining the amount of chelated metal cation released wherein the amount of chelated metal cation released is indicative of the disruption of the chelated metal cation domain.
- 10 2. A method according to claim 1 wherein the metal is zinc.
3. A method according to claim 2 wherein the release of zinc is determined by a change in fluorescence of a zinc-selective fluorophore.
- 15 4. A method according to claim 3 wherein the fluorophore is TSQ.
5. A method of identifying compounds useful in the treatment of a disease condition caused or exacerbated by an MPV comprising contacting a protein molecule containing a  
20 chelated metal cation domain, encoded by an MPV gene, with an effective amount of said compound for a time and under conditions sufficient to facilitate disruption of the chelated metal cation domain and directly or indirectly determining the absence or otherwise of binding of said protein to a ligand, wherein the absence of binding is indicative of disruption of the chelated metal cation domain.
- 25 6. A method according to claim 5 wherein the ligand is E6AP, E6BP, paxilin or similar or homologue motifs.
7. A method according to claim 1 or 5 wherein the MPV is an HPV.

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AMENDED SHEET  
IPEA/AU

- 51 -

8. A method according to claim 7 wherein the HPV is selected from HPV-6, HPV-11, HPV-16, HPV-18.

9. A method according to claim 8 wherein the HPV is HPV-16.

5

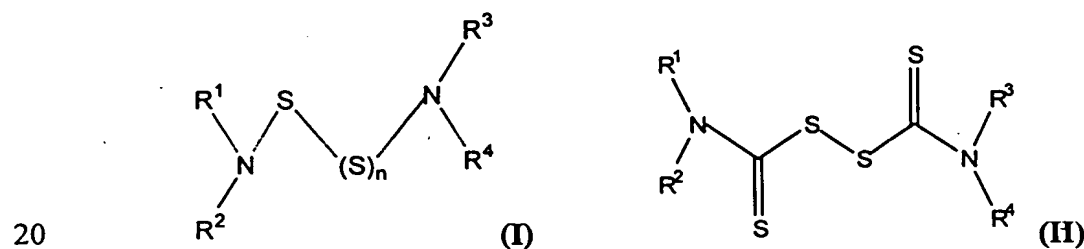
10. A method according to claim 9 wherein the protein is the HPV-16 E6 or E7 oncoprotein.

11. A method according to claim 8 wherein the HPV is HPV-18.

10

12. A method according to claim 11 wherein the protein is the HPV-18 E6 or E7 oncoprotein.

13. A method of treating or preventing a disease condition caused or exacerbated by an MPV comprising the administration of an effective amount of a compound capable of facilitating the disruption of a chelated metal cation domain of a protein encoded for by an MPV gene to a mammal in need thereof, wherein the compound is of general formula (I) or (II):



wherein

n is selected from 1-5

25 R<sup>1</sup> - R<sup>4</sup> are independently selected from hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally



- 52 -

substituted arylalkyl optionally substituted acyl, optionally substituted heterocyclyl, halo alkyl, arylalkyl, carboxy, carboxy ester and carboxamido; or

R<sup>1</sup> and R<sup>2</sup> together, and/or R<sup>3</sup> and R<sup>4</sup> together, independently form a group of formula

5 (a):



wherein: U is selected from CH<sub>2</sub>, O, NH or S;

10 l and n are independently selected from 0 to 6 and m is 0 or 1 when U is CH<sub>2</sub> and m is 1 when U is O, NH or S, such that

l+m+n is greater than or equal to 2;

and wherein any one or more (CH<sub>2</sub>) or NH groups may be further optionally substituted.

15

14. A method according to claim 13 wherein R<sup>1</sup> and R<sup>2</sup> together, and/or R<sup>3</sup> and R<sup>4</sup> together, independently form a group of formula (a):



20

wherein: U is selected from CH<sub>2</sub>, O, NH or S;

l and n are independently selected from 0 to 6 and m is 0 or 1 when U is CH<sub>2</sub> and m is 1 when U is O, NH or S, such that

l+m+n is greater than or equal to 2;

25

and wherein any one or more (CH<sub>2</sub>) or NH groups may be further optionally substituted.

15. A method according to claim 14 wherein U is CH<sub>2</sub>.

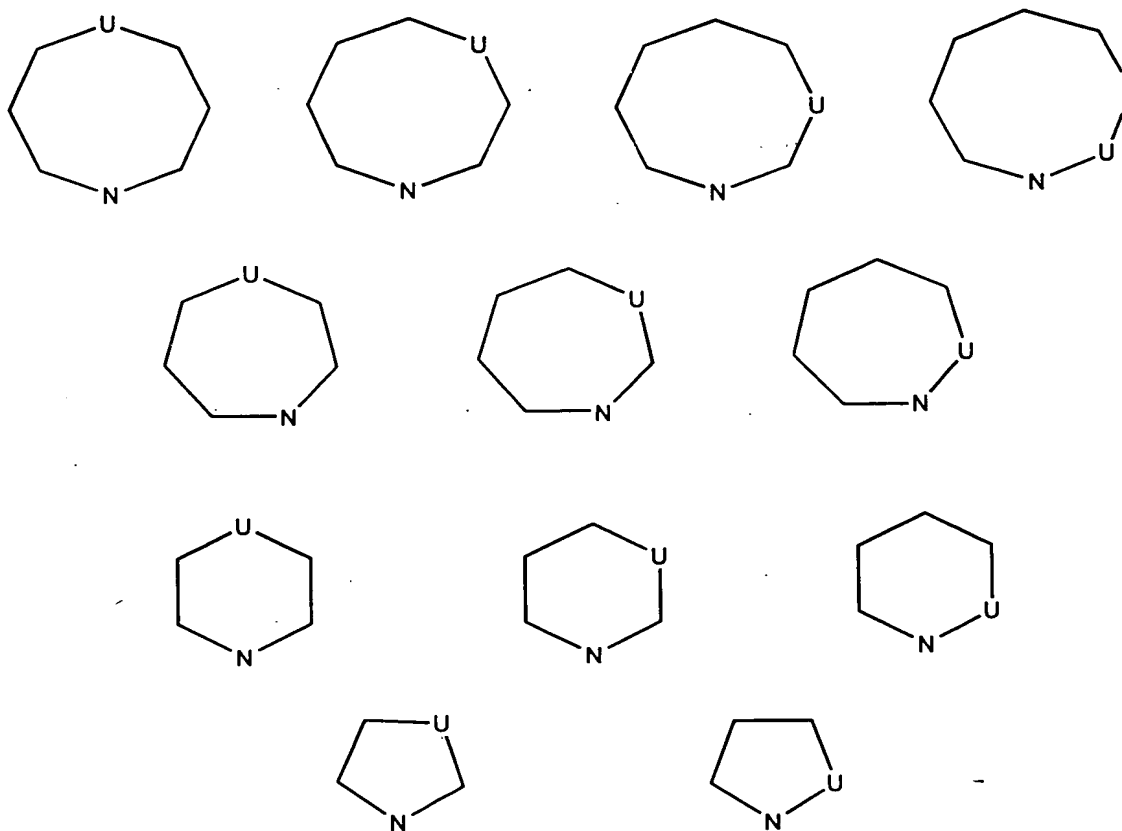
- 53 -

16. A method according to claim 15 wherein formula (a) is selected from one of -  $(CH_2)_2$ -,  $-(CH_2)_3$ -,  $-(CH_2)_4$ -,  $-(CH_2)_5$ -,  $-(CH_2)_6$ - or  $-(CH_2)_7$ -.

17. A method according to claim 14 wherein U is NH, O, or S and m is 1.

5

18. A method according to claim 14 wherein  $R^1$  and  $R^2$ , and/or  $R^3$  and  $R^4$ , together with the nitrogen to which they are attached independently form a group selected from:



10 which may be optionally substituted at a carbon atom, and/or where U is NH, at the nitrogen atom.

AMENDED SHEET  
IPEA/AU

- 54 -

19. A method according to claim 18 wherein R<sup>1</sup> and R<sup>2</sup>, and/or R<sup>3</sup> and R<sup>4</sup>, together with the nitrogen to which they are attached each independently form an optionally substituted morpholino, thiomorpholino, or piperazino group.

5 20. A method according to any one of claims 14 to 19 wherein any -CH<sub>2</sub>- group of formula (a) is optionally substituted by one or more of the groups selected from methyl, ethyl, n-propyl, iso-propyl, hydroxy, halo, methoxy, ethoxy, iso-propoxy, acetoxy, optionally substituted benzyl, optionally substituted pyridyl, optionally substituted pyrimidyl and optionally substituted phenyl.

10

21. A method according to claim 13 wherein at least one of R<sup>1</sup> - R<sup>4</sup> is independently selected from: hydrogen, optionally substituted phenyl, optionally substituted cyclopropyl, optionally substituted cyclobutyl, optionally substituted cyclopentyl, optionally substituted cyclohexyl, formyl, acetyl.

15

22. A method according to claim 21 wherein the optional substituent is selected from the groups methyl, ethyl, n-propyl, iso-propyl, hydroxy, halo, methoxy, ethoxy, iso-propoxy, acetoxy, and phenyl.

20 23. A method according to claim 13 wherein at least one of R<sup>1</sup>-R<sup>4</sup> is as depicted in any compound in Groups 1 to 6 as defined herein.

24. A method according to claim 13 wherein n is selected from 1, 2 or 3, preferably 1 or 2.

25

25. A method according to claim 13 wherein the MPV is an HPV.

26. A method according to claim 25 wherein the HPV is selected from the group consisting of HPV-1, 2, 3, 4, 6, 11, 16, 18, 27, 31, 33, 35, 45 and 57.

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- 55 -

27. A method according to claim 26 wherein the HPV is HPV-16.

28. A method according to claim 27 wherein the protein is the HPV-16 E6 or E7 oncoprotein.

5

29. A method according to claim 26 wherein the HPV is HPV-18.

30. A method according to claim 29 wherein the protein is the HPV-18 E6 or E7 oncoprotein.

10

31. A method according to claim 13 where the chelated metal cation domain is a chelated zinc cation domain.

32. A method according to claim 31 wherein the chelated zinc domain is the sequence  
15 motif cys-X2-cys-X29-cys-X2-cys.

33. A method of treating or preventing a disease condition caused or exacerbated by an MPV comprising the administration of an effective amount of a compound as defined in claim 13 to a mammal in need thereof.

20

34. A method according to claim 13 or 33 wherein the compound is capable of effecting at least 30% zinc release in a TSQ assay and/or inhibits or reduces the binding of an E6 protein to E6AP or E6BP and/or exhibits selective cytotoxicity towards MPV-infected cells.

25

35. A method according to claim 13 or 33 wherein the disease or condition is cervical cancer or its HPV associated precursor lesions or any other HPV associated cancers and/or warts.

- 56 -

36. A composition comprising a compound capable of facilitating the disruption of a chelated metal cation domain of a protein encoded for by an MPV gene, together with a pharmaceutically acceptable carrier, diluent or excipient wherein the compound is of general Formula (I) or (II) as defined in claim 13.

5

37. Use of a compound capable of facilitating the disruption of a chelated metal cation domain of a protein encoded for by an MPV gene in the manufacture of a medicament for the treatment or prophylaxis of a disease or condition caused or exacerbated by a MPV, wherein the compound is of general Formula (I) or (II) as defined in claim 13.

10

38. Use of at least one compound of general formula (I) or (II) as defined in claim 13 in the manufacture of a medicament for the treatment or prophylaxis of a disease or condition caused or exacerbated by an MPV.

15

39. An agent useful in the treatment or prophylaxis of a disease condition caused or exacerbated by an MPV, said agent comprising a compound capable of reducing, inhibiting or otherwise decreasing the activity of a protein encoded by an MPV gene where said agent facilitates disruption of a chelated metal cation domain present in said protein, wherein the compound is of general formula (I) or (II) as defined in claim 13.

20

40. A method of treating or preventing a disease condition caused or exacerbated by an MPV comprising the administration of an effective amount of a compound capable of facilitating the disruption of a chelated metal cation domain of a protein encoded for by an MPV gene to a mammal in need thereof, wherein said compound is a compound identified in accordance with the method of claim 1.

25

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU 99/00724

**A. CLASSIFICATION OF SUBJECT MATTER**

Int Cl<sup>6</sup>: C07D 203/24, 205/04, 207/48, 209/48, 211/96, 213/76, 239/28, 239/42, 243/08, 263/04, 265/30, 295/194, 295/26, 317/58; C07C 323/49, 333/32, 381/00; A61K 31/13, 31/145, 31/535, 31/55

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

- 1 STN Substructure and Keyword Search: Substructure and papilloma? and (viral or virus)  
 2 WPIDS: Substructure, not polymer? zinc? pharmaceutical? or medic?

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X 1	Derwent Abstract Accession No: 92-303542/37, B05, JP 4-208223, 27 July 1992 (KAWAGUCHI KAGAKU KOGYO KK)	1-21,23,24,61,63-74,76,77
X 2	Synlett, August 1990, pages 473-476 (KATRITZKY, Alan R et al) "The Synthesis of Bis(N,N-disubstituted amino) Trisulphides" see page 473 column 2	1-21,23,24,61,63-74,76,77

☒ Further documents are listed in the continuation of Box C

☒ See patent family annex

* Special categories of cited documents:	
"A" Document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search  
07 October 1999

Date of mailing of the international search report  
25 OCT 1999

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU 99/00724

C (Continuation).

## DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X 3	Derwent Abstract Accession No: 95-340184/44, B05 (B03) JP 7-233057 A (KINKI DAIGAKU GH), 5 September 1995	1-9,22-24,61,63,75,77
X 4	Brain Research volume 44 No: 2 (1972), pages 603-613 (LYCKE, E et al) "The Monoamine Metabolism in Viral Encephalitides of the Mouse II, Turnover of Monoamines in Mice Infected with Herpes Simplex Virus" page 604, line 17	1-9,22-24,61,63,75,77
X 5	Derwent Abstract Accession No: 86-282536/43, B03, C02, JP 1207376 A (TOYO SODA MFG KK), 13 September 1986	1-9,22-24,61,63,75-77
X 6	Derwent Abstract Accession No: 88-245781/35 A12, JP 3-178148 A (NIPPON OIL SEAL IND) 22 July 1988	1-9,22-24,61,63,75-77
X 7	Derwent Abstract Accession No: 91-038784/05 S03, JP 2-304346 A (NIHON PARKERIZING) 18 December 1990	1-9,22-24,61,63,75-77
X 8	Derwent Abstract Accession No: 91-122584/17 B03, JP 3-063258 A (KURARAY KK) 19 March 1991	1-9,22-24,61,63,75-77
X 9	EP 562750 (BRIDGESTONE CORPORATION) 29 September 1993 page 3 lines 5-52, page 8 lines 12-14	1-9,22-24,61,63,75-77
X 10	Virology volume 243, pages 287-292 (1998) (OTT, David E et al) "Inhibition of Friend Virus Replication by a Compound that Reacts with the Nucleocapsid Zinc Finger: Anti-Retroviral Effect Demonstrated in Vivo" abstract; fourth, fifth, tenth and twelfth compounds of Table 1 Formula (II)	1-9,22-24,37-45,58-60,62,63,75-83
X 11	Journal of Medicinal Chemistry, volume 40 No: 13 (1997) pages 1969-1976 (McDONNELL, Nazli, B et al) "Zinc Ejection as a New Rationale for the Use of Cystamine and Related Disulfide-Containing Antiviral Agents in the Treatment of AIDS" abstract; figures 1, 2; Table 1; page 1973 last paragraph to page 1974 first paragraph Formula (I)	1-9,22-24,37-45,58-60,62,63,75-83
X 12	Techniques in Protein Chemistry VIII [Symp Protein Soc], 10 <sup>th</sup> (1997), Meeting Date 1996, pages 231-244 (CHERTOVA, E et al) "Reaction of HSV-1 NC p7, Zinc Fingers with Electrophilic Reagents" pages 231-232, 235-237, 241-242 Formula (I)	1-9,22-24,37-45,58-60,62,63,75-83

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X 13	WO 96/09406 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA, REPRESENTED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES) 28 March 1996 abstract, pages 4-6, claims 1 and 7 <i>formula II</i>	1-9,22-24,37-45,58-60,62,63,75-83
X 14	Drug Metabolism and Disposition: The Biological Fate of Chemicals, volume 24 No: 12 (1996), pages 1395-1400 (HATHOUT, Yetrib et al) "Characterisation of Intermediates in the Oxidation of Zinc Fingers in Human Immunodeficiency Virus Type I Nucleocapsid Protein P7" abstract, figure 1, page 1397 column 1 second paragraph, page 1398 column 2 second paragraph <i>formula II</i>	1-9,22-24,37-45,58-60,62,63,75-83
X 15	Journal of Medicinal Chemistry, volume 39 No: 19 (1996) pages 3606-3616 (RICE, William G et al) "Evaluation of Selected Chemotypes in Coupled Cellular and Molecular Target-Based Screens Identifies Novel HIV-1 Zinc Finger Inhibitors" abstract, page 3608 column 2 last paragraph, Table 10 <i>formula II</i>	1-9,22-24,37-45,58-60,62,63,75-83
X 16	Journal of Virology, volume 70, No: 8 (1990) pages 4966-4972 (REIN, Alan et al) "Inactivation of Murine Leukemia Virus by Compounds that React with the Zinc Finger in the Viral Nucleocapsid Protein" abstract, page 4970 first paragraph <i>formula II</i>	1-9,22-24,37-45,58-60,62,63,75-83
X 17	Carcinogenesis, volume 9, No: 9 (1988) pages 1547-1551 (ROTSTEIN, Joel B et al) "Effect of Exogenous Glutathione on Tumour Progression in the Murine Skin Multistage Carcinogenesis Model" abstract, page 1547 last paragraph to page 1548 first paragraph, page 1549 first paragraph, figure 2 <i>formula II</i>	1-9,22-24,37-45,58-60,62,63,75-83
X 18	Chemical Abstracts 102:8009 Rubber Chem Technol (1984), volume 57 No: 4 pages 744-754 RN 86796-75-0 86796-78-3 86796-79-4	1-21,23,24,63-74,76,77
X 19	Chemical Abstracts 111:146042 Chromatographia (1989) volume 27 No: 3-4 pages 113-117 RN 122756-65-4	1-21,23,24,63-74,76,77
X 20	Chemical Abstracts RN 95255-69-9	1-21,23,24,63-74,76,77
X 21	Chemical Abstracts RN 103-34-4	1-21,23,24,63-74,76,77



# INTERNATIONAL SEARCH REPORT

International application No.

**PCT/AU 99/00724**

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report			Patent Family Member				
JP	4-208223	NONE					
JP	7-233057	US	5665770	US	5874455		
JP	1-207376	JP	63-302533				
JP	3-178148	NONE					
JP	2-304346	NONE					
JP	3-63258	NONE					
EP	562750	DE	69314208	ES	2110053	JP	5262916
		US	5391635				
WO	96/09406	AU	35927/95	EP	782632		